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PRINCIPAL INVESTIGATOR: Mariana Morris, PhD

CONTRACTING ORGANIZATION: Wright State University
Dayton, OH 45435

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14. ABSTRACT The goal of the GWI consortium is to develop a better understanding of GWI and identify specific disease targets to find treatments that will address the cause of the disease and not just treat the symptoms associated with the disease. Current treatments used for GWI only treat the symptoms associated with the disease and do not target the underlying disease process. This consortium will integrate our clinical understanding of the disease process with basic research efforts using a novel mathematical model. This mathematical model or computational biology approach will enable the consortium to quickly identify targets of dysfunction and find treatments that will address the causes of the disease. In an effort to quickly identify disease targets and find effective GWI treatments, this consortium uses a computational biology approach that combines data derived from animal models of GWI and humans. Our approach takes into account several alternatives, with different targets. By using this approach, the consortium will create a short list of attractive known and FDA-approved drugs that could be tested rapidly in clinical trials without requiring a drug development effort. However, we will also be able to identify highly effective disease targets that could also lead to drug development. By increasing the understanding of the reasons for GWI, our consortium will advance the diagnosis and treatment of the disease. Specifically, our more detailed understanding of the dysfunction involved in GWI would greatly increase the speed to identify targets for improved diagnosis as well as selection and testing of more specific treatments over the longer term that will address the causes of disease. The goal of this development project is to develop a research team to produce cutting edge research on GWI.					
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TABLE OF CONTENTS

Front Cover	
Report Document	1
Introduction	2
Body	4
Key Research Accomplishments	5
Conclusions	5

INTRODUCTION

Gulf War Illness (GWI) is a condition associated with a diverse array of symptoms that include debilitating fatigue, memory and cognition difficulties, headaches, sleep disturbances, gastrointestinal problems, skin rashes, as well as musculoskeletal/joint pain. The diversity of the symptoms suggests the involvement of multiple organ systems. Indeed, a number of studies of GWI report involvement of the central and autonomic nervous systems, the immune system as well as multiple endocrine systems including the thyroid, reproductive organs and adrenal. Due to the non-specific and general nature of symptoms associated with GWI, disturbances in one or more systems or at various levels of a given system may be occurring.

The underlying mechanisms of this disease remains unknown and treatment has been palliative, symptom-driven and physician-directed, because there are no specific treatment guidelines or biomarkers of the syndrome. It is proposed that the multi-system nature of GWI requires an overreaching multi-disciplinary, -institutional and -investigator approach to identify and define therapeutic targets. Therefore, the overall goal of our consortium is to combine our clinical understanding of the disease and basic research efforts using a computational biology approach based on systems biology to pinpoint underlying mechanisms of disease and target treatment more effectively. Specifically, our more detailed understanding of the dysfunction associated with key metabolic pathways involved in GWI would greatly expedite the identification of promising biomarkers for diagnosis as well as selection and testing of more targeted therapeutic interventions over the longer term that will address the underlying mechanisms of disease. The development grant was a major success since it brought together a talented and diverse group of scientists and research labs with the capability of attacking the problem of gulf war illness

BODY

The goal of the consortium was to develop an infrastructure for the establishment of a scientific research consortium which focused on Gulf War Illness (pathobiology and treatment). The group established a multidisciplinary and multi institutional team (8 sites with 13 scientists).The program established a goal of computational modeling of biomarkers (immune, autonomic and endocrine) with animal and clinical tests.

Consortium Organization

The team gathered in one central location at two different times. This was to establish concepts and objectives of the consortium. Table 1 lists the meeting dates, purpose of the meetings, and who attended. This led to a successful preparation of a GWI consortium grant

Table 1. List of meetings, where they were held, the purpose of the meeting and attendees.

Date	Where	Purpose	Attendees
December 2-3, 2011	San Antonio, TX	purpose of making progress on the grant set timelines	Morris, Lucot, Nahhas, Gutierrez, McDonough, O'Callaghan, Miller, Klimas, Fletcher, Broderick, Eells, Chambers, Steele, Helton
August 12-14, 2011	Hernandon, FL	to divide in groups and setup objectives	Morris, Lucot, Gutierrez, O'Callaghan, Miller,

			Klimas, Broderick, Eells, Helton, Fletcher
April 9-11, 2012	Miami, FL	GWIC Grant meeting to start grant	Morris, Klimas, Fletcher, O'Callaghan, Broderick

There were a large number of people involved in the writing, development, and organization of the consortium. Table 2 lists everyone that was involved in writing, data gathering, experiment organization, and overall planning of the grant. In addition to those who are investigators on the grant, a grant writer was hired to edit and assist with the writing. A grant administrator was also used to organize the large group of people and gather the required information for grant submission.

Table 2. List of personnel involved in analysis, writing and grant structure

BASIC SCIENCES CORE: MORRIS, DIRECTOR			
Institution	Investigators	Research Area	Role
Wright State University Boonshoft School Medicine	Marianna Morris	GWIC Animal Models Autonomic Pharmacology	Co-Principal Investigator
Wright State University Boonshoft School Medicine	James Lucot	Behavior Autonomic measures	Co-Investigator
Center Disease Control	James O'Callaghan	GWIC Animal Models	Co-Investigator
Center Disease Control	Diane Miller	Neuroimmunology, HPA actions	Co-Investigator
CLINICAL SCIENCES CORE: KLIMAS, DIRECTOR			
NOVA Southeastern University Miami VA Medical Center	Nancy Klimas	GWIC Clinical Profiling, Access to GWIC Clinical Population	Co- Principal
Baylor University	Lea Steele	Preclinical Protocols Epidemiology	Co-Investigator
Miami VA Medical Center	MaryAnn Fletcher	Clinical and mouse laboratory assays	Co-Investigator
COMPUTATIONAL SCIENCES CORE: BRODERICK, DIRECTOR			
University Alberta	Gordon Broderick	Data Analysis and Modeling	Co-Principal
Wright State University	Miryoung Lee	Data Management Statistical Analysis	Co-Investigator

DRUG DEVELOPMENT CORE: MCDONOUGH, DIRECTOR			
Southwest Research Institute	Joe McDonough	Drug Formulation & Development	Co-Investigator
Epiomed Therapeutics	David Helton	Drug Development & Experimental Design	Consultant
Southwest Research Institute	Gloria Gutierrez	Clinical Trial Support Drug Discovery	Co-Investigator
ADMINISTRATION			
Wright State University	Teresa Garrett	Organization/Administration/Writing	
NOVA	Beth Gilbert	Grant Writing	

Grant Submission

The grant “Understanding Gulf War Illness: An Integrative Modeling Approach” was submitted on June 15, 2012.

KEY RESEARCH ACCOMPLISHMENTS

- Established list of accomplished scientists to commit to work
- Establishment of core research groups for consortium work

CONCLUSION

This consortium consists of leading scientific experts with a focus that is complementary, related to, or focused on GWI. This team combines researchers with expertise in basic and clinical research along with those with expertise in drug development, formulation and testing. Under the leadership of, Drs. Mariana Morris, Nancy Klimas and Gordon Broderick, the team is expert in neurotoxicology, autonomic pharmacology, animal modeling, computational modeling, clinical research, drug development and drug repurposing. There are four cores that contribute to the overall goal of the consortium including a basic science core, clinical science core, computational core and therapeutic science core. Together, this integrated consortium will provide the best opportunity for advancing GWI diagnosis and treatment.

Conventional GWI treatments have failed to effectively treat the underlying dysfunction associated with GWI, aside from managing symptomatology. This consortium will pinpoint underlying mechanisms of disease and target treatment more effectively in order to re-establish homeostatic function. Specifically, our more detailed understanding of the dysfunction associated with key metabolic pathways involved in GWI would greatly expedite the identification of promising biomarkers for diagnosis as well as selection and testing of more targeted therapeutic interventions over the longer term that will address the underlying mechanisms of disease.